Membrane organization of the dystrophin-glycoprotein complex.

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The stoichiometry, cellular location, glycosylation, and hydrophobic properties of t components in the dystrophin-glycoprotein complex were examined. The 156, 59, 43, and 35 kd dystrophin-associated proteins each possess unique antigenic determinants, enrich quantitatively with dystrophin, and were localized to the skele muscle sarcolemma. The 156, 50, 43, and 35 kd dystrophin-associated proteins contained Asn-linked oligosaccharides. The 156 kd dystrophin-associated glycopr contained terminally sialylated Ser/Thr-linked oligosaccharides. Dystrophin, the 1: kd, and the 59 kd dystrophin-associated proteins were found to be peripheral membrane proteins, while the 50 kd, 43 kd, and 35 kd dystrophin-associated glycoproteins and the 25 kd dystrophin-associated protein were confirmed as integ membrane proteins. These results demonstrate that dystrophin and its 59 kd associa protein are cytoskeletal elements that are tightly linked to a 156 kd extracellular glycoprotein by way of a complex of transmembrane proteins.

PMID: 1913804 [PubMed - indexed for MEDLINE]

1: Cancer Invest 1999;17(1):10-18 Related Articles, Books, Link

Influence of antiestrogens on the invasiveness and laminin attachm of breast cancer cells.

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Metastatic spread of breast cancer is responsible for most of the morbidity and mortality associated with this disease. Thus, it is important to identify agents with antimetastatic activity. Because invasiveness and tumor cell attachment are fundamental steps in the metastatic cascade, the major objective of the present stuc was to evaluate the antimetastatic potential of three antiestrogens, each with differe chemical structure and mechanism of action, on breast cancer cell invasiveness anc laminin attachment. The antiestrogens examined were tamoxifen, a mixed antagonist/agonist; Analog II, a cyclopropyl antiestrogen with pure antagonist activ and ICI-182,780, a steroidal antiestrogen with pure antagonist activity. Our results indicate that MDA-MB-231 human breast cancer cells are much more invasive anc have a higher affinity for laminin than do MCF-7 human breast cancer cells. All th antiestrogens, at a concentration of 10(-6) M, produced a reduction in MDA-MB-2 cell invasiveness, which was comparable in magnitude to their inhibition of MDA-MB-231 attachment to laminin. Evaluation of MDA-MB-231 cell morpholo using scanning electron microscopy revealed the involvement of cellular pseudopo and microvilli in the process of invasion. The results of this study suggest that antiestrogen-induced inhibition of breast cancer cell invasiveness could be due in p to a decrease in the attachment of tumor cells to laminin in the basement membran

PMID: 10999044 [PubMed - indexed for MEDLINE]

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Evaluation of serum laminin as a tumor marker in breast cancer.

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Laminin is a noncollagenous constituent of the extracellular matrix (basement membrane). Increased serum concentrations were recorded in patients with a variet cancers. The clinical usefulness of serum laminin as a marker for breast cancer wa: investigated in 60 female patients with malignant breast tumors (30 metastatic, 30 non-metastatic). Subjectively healthy age-matched women (n = 30) served as a con group. Laminin was significantly higher in breast cancer patients than in normal controls. Serum laminin levels were also significantly higher in patients with metastasis than in those without metastasis. A positive correlation was observed between serum laminin and the breast cancer-associated antigen CA 15-3 in the tu patients. The sensitivity and specificity values of laminin for cancer detection at th optimum decision level [mean + 2 SD (1.4 U/ml)] were 75% and 97% respectively with a 98% positive predictive value, 66% negative predictive value, and 82% diagnostic efficiency. For the detection of metastasis, serum laminin exhibited 77% sensitivity and 100% specificity [best decision level: mean + 2 SD (1.9 U/ml)], wit 100% positive predictive value, 81% negative predictive value, and 88% diagnosti efficiency. The latter specificity and positive predictive value were superior to thos obtained with serum CA 15-3. These results suggest that serum determination of laminin could be a useful diagnostic tool in breast cancer and a valuable parameter the prediction of metastasis.

Publication Types:
- Clinical trial

PMID: 10356660 [PubMed - indexed for MEDLINE]